ACRIN Experience with Quantitative PET

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ACRIN Background

ACRIN™ American College of Radiology Imaging Network

- NCI funded collaborative group with a mission to perform multicenter trials of imaging
- Originally funded in 1999
- Accrued over 75,000 patients in over 25 trials at over 100 sites
- Trials of image detection, characterization, therapeutic guidance, monitoring (including clinical outcomes)
- Trials including multiple modalities: CT, MR, PET, SPECT, Mammography, and Ultrasound

ACRIN Studies that include quantitative PET

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Study #	Target	Agent	Status	Accrual
6665	GIST	FDG	Follow up	63
6668	NSCLCA	FDG	Follow up	251
6671	Cervical	FDG	Open	50
6678	NSCLCA	FDG	Open	60
6682	Cervical	Cu ATSM	Open	5
*6684	Glioma	FMISO	Open	1
6685	H & N	FDG	Ready to Open	-
*6687	Prostate (bone)	^{18}F	Open	2
*6688	Breast	FLT	Open	3
*6689	Glioma	FLT	Ready to Open	-
4003/4	Alzheimer's	PIB, FPIB,AV45	Open	31

Imaging Core Laboratory

*Performed under NCI sponsored IND

Lessons Learned

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- **Quality Control**
  - Qualification
  - Ongoing Quality Control
- **Accrual**
  - Site recuritment
- **Trial Design/Qualification Strategy**

ACRIN Site Qualification

- **Establish Site Infrastructure**
  - ACR accreditation or demonstration of proper technology/personnel (Only complete ring dedicated PET scanners)
- **Uniform Phantom Images**
- **2 Sample Clinical Images using ACRIN acquisition Protocol**

148 sites have been qualified

Uniform Phantom Results

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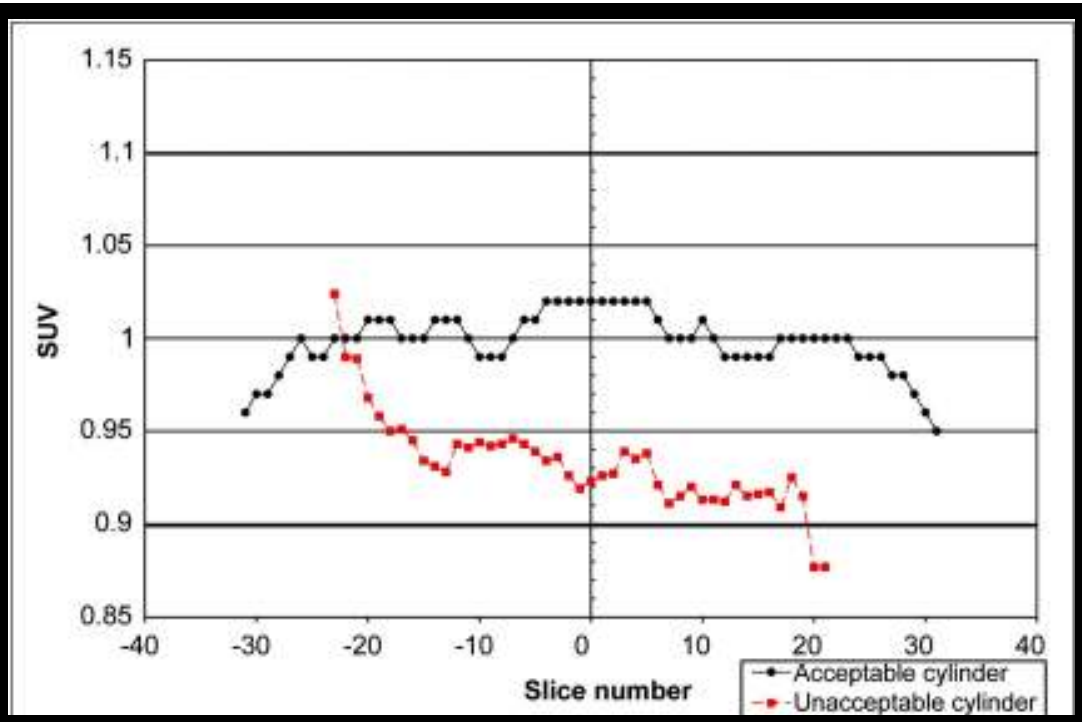
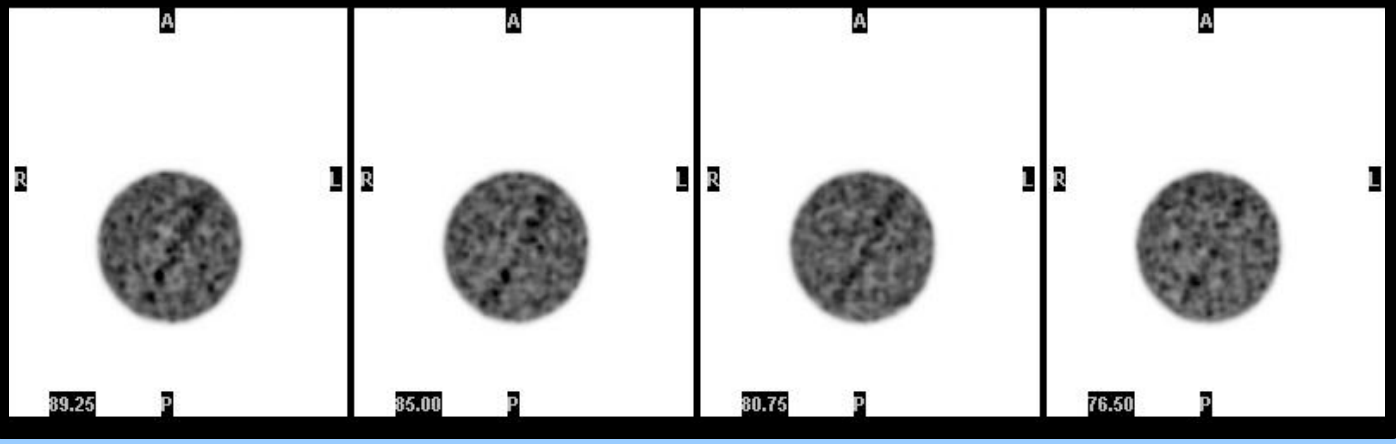
Problem	Submission date, June 2005–December 2006 (n = 53)	Submission date, May 2007–June 2008 (n = 48)
Overanonymization of DICOM header	0 (0)	4 (0)
Incorrect information in DICOM header/on application	15 (1)	10 (0)
Clock synchronization problem	6 (0)	4 (0)
Incomplete application	2 (1)	3 (0)
Improper data format	7 (1)	1 (0)
Image display problem	0 (0)	1 (0)
Normalization calibration	5 (1)	1 (1)
SUV calibration	1 (0)	5 (3)
Total	36 (4)	29 (4)

Scheuermann et al J Nucl Med. 2009 Jul;50(7):1187-93

Typical Calibration Problem





Categories of Failures

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- Some information in the DICOM header needs to be edited
  - Incorrect weight for a phantom
  - Typo while entering weight, dose, or dose assay time
  - Failing to compensate for time difference between dose calibrator and scanner
  - Failing to account for residual activity in syringe
- New data must be acquired and submitted to ACRIN
  - Uncertainty about the time or amount of injection
  - Failure to record and account for residual activity in syringe
- Some or all of the calibrations on the scanner must be redone and new application submitted to ACRIN

Ongoing Image Quality Control

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- Image and header review to assess protocol compliance, with timely intervention to correct problems at individual sites
- Protocol-specific image quality control
  - Ongoing monitoring of instrument performance
  - Site and core-laboratory radiologist review of submitted images
  - Quantitative assessments (e.g., reference-tissue SUV)
- Typically greater than 90% acceptable data quality
  - Most common problem is imaging out time window

Analysis

$$\textbf{SUV} = \frac{\text{tissue conc. (μCi/gm)}}{\text{inj. dose (μCi)/body weight (gm)}}$$

SUV_{max} = Maximum SUV within the ROI (tumor)

- Single voxel
- Automated process

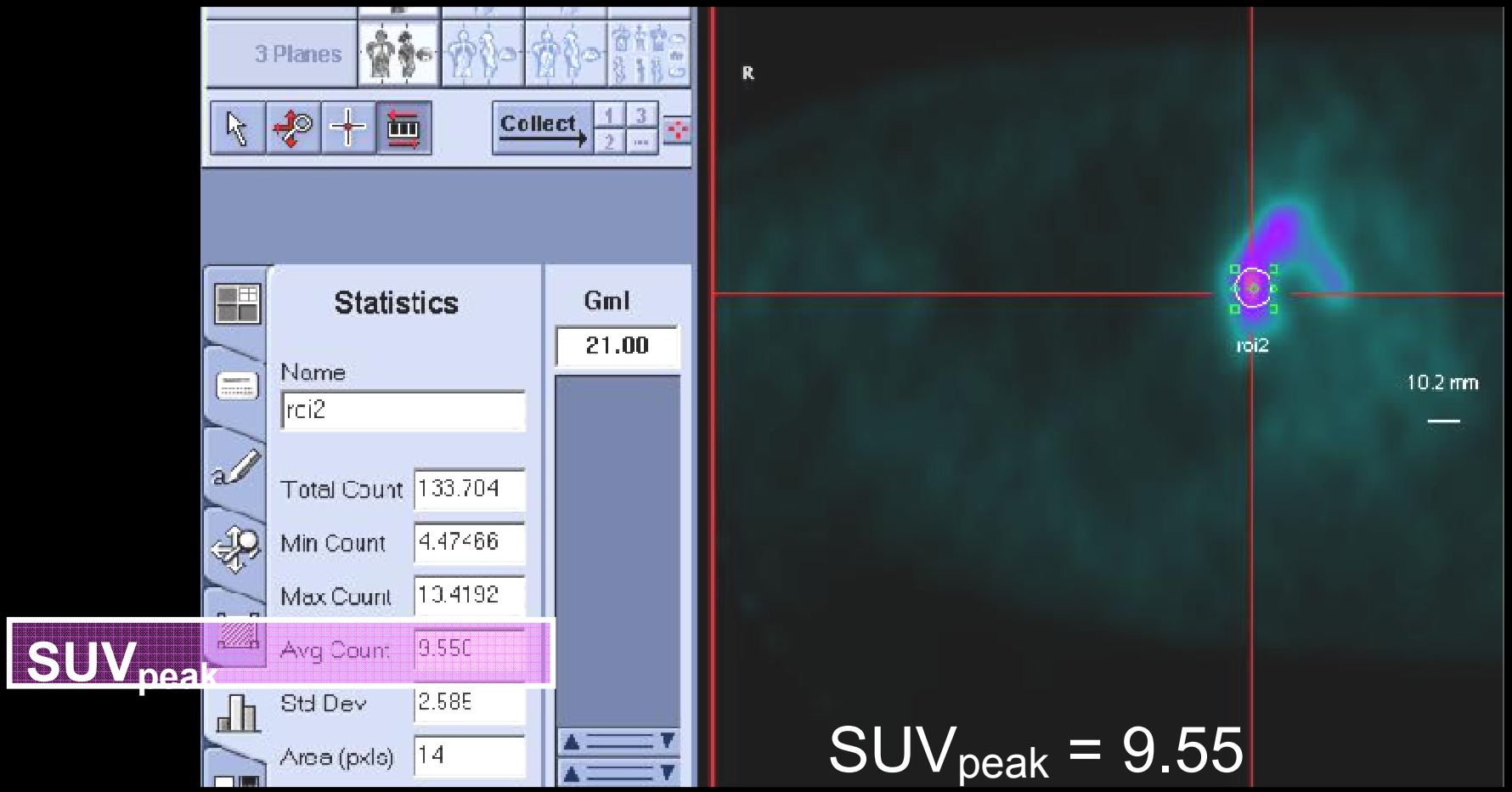
SUV_{peak} = Mean SUV in 0.75-1.5 cm (ideally 1.0 cm)

diameter ROI "centered" on SUV_{max}

- Partially manual, partially automated process

Determining the SUV_{peak}

- **Read the average SUV within the circular 0.75-1.5 cm ROI.**



Pre-treatment Primary Tumor

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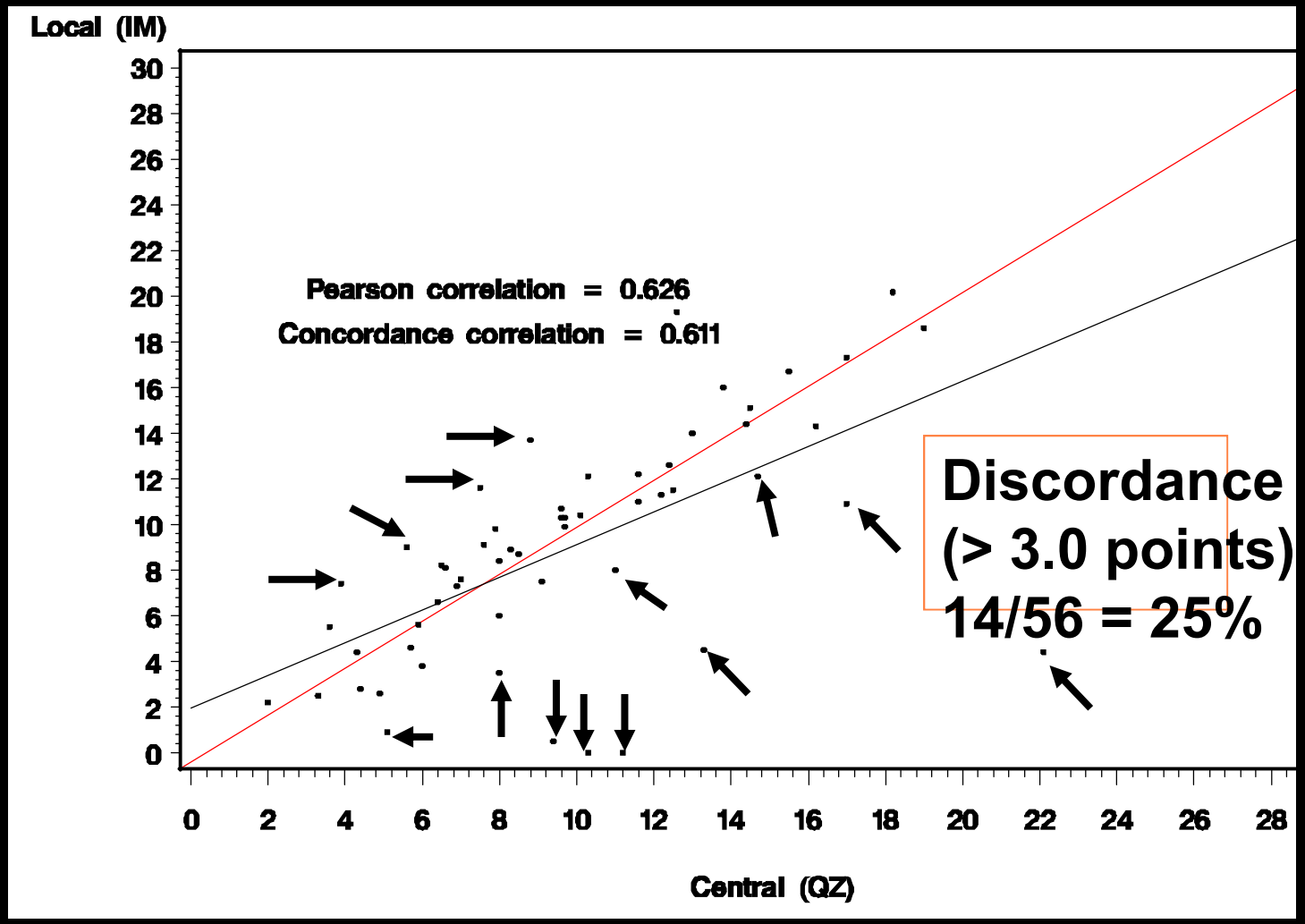
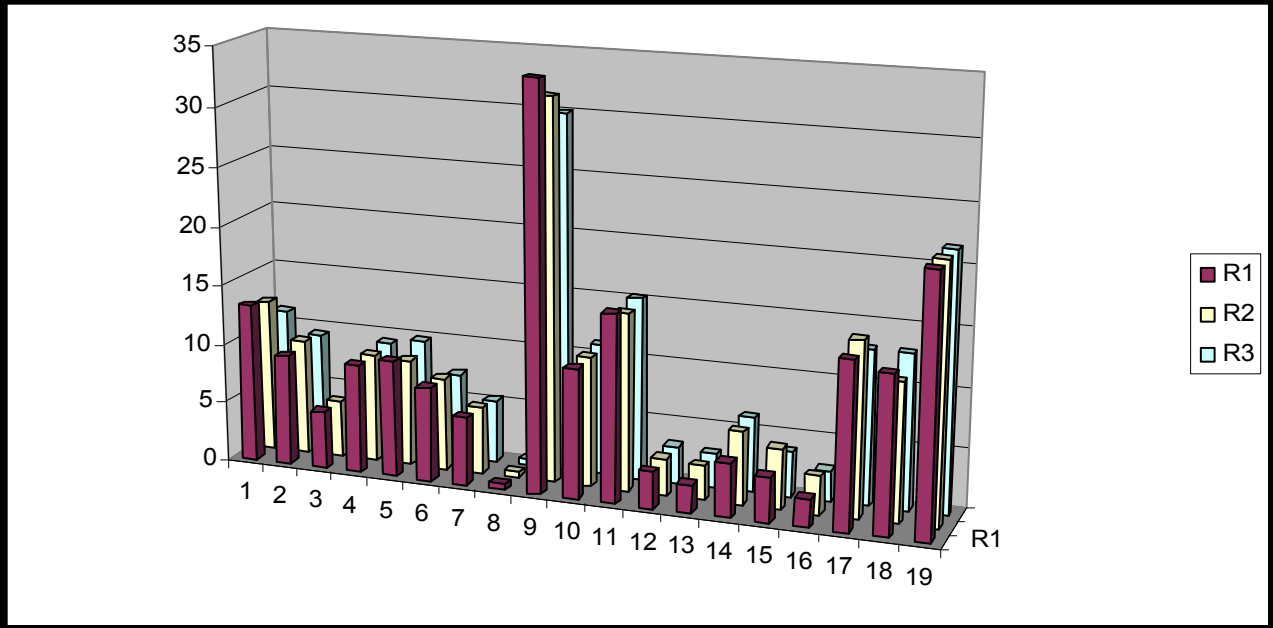
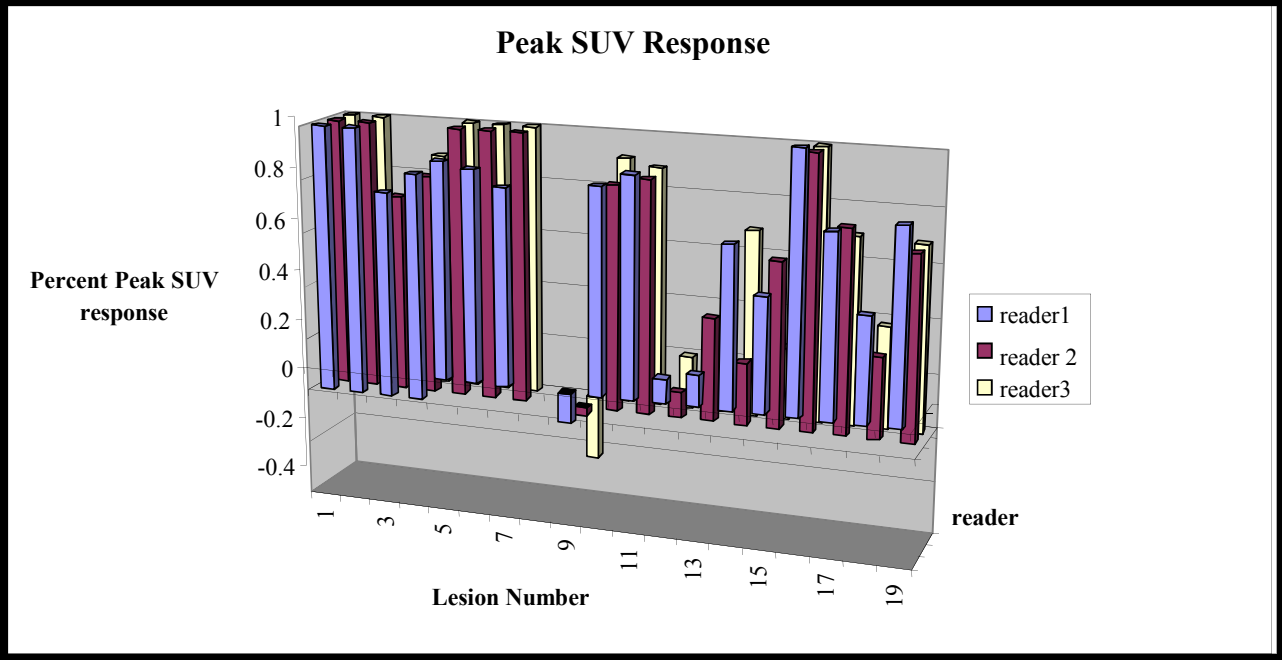
Correlation between Local and Central SUV's



Peak SUV measurement by Reader



The average core lab standard deviation between readers for measurement of the Peak SUV was .5 units



The average core lab standard deviation between readers for measurement of the percent response was 7% for peak SUV

Primary PET Biomarker Imaging Trials: Unique Accrual Issues

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- **No immediate patient benefit**
- **Radiation Concerns**
- **Scheduling issues**
- **Site recruitment**
  - The "Venn Diagram" problem

Site Recruitment

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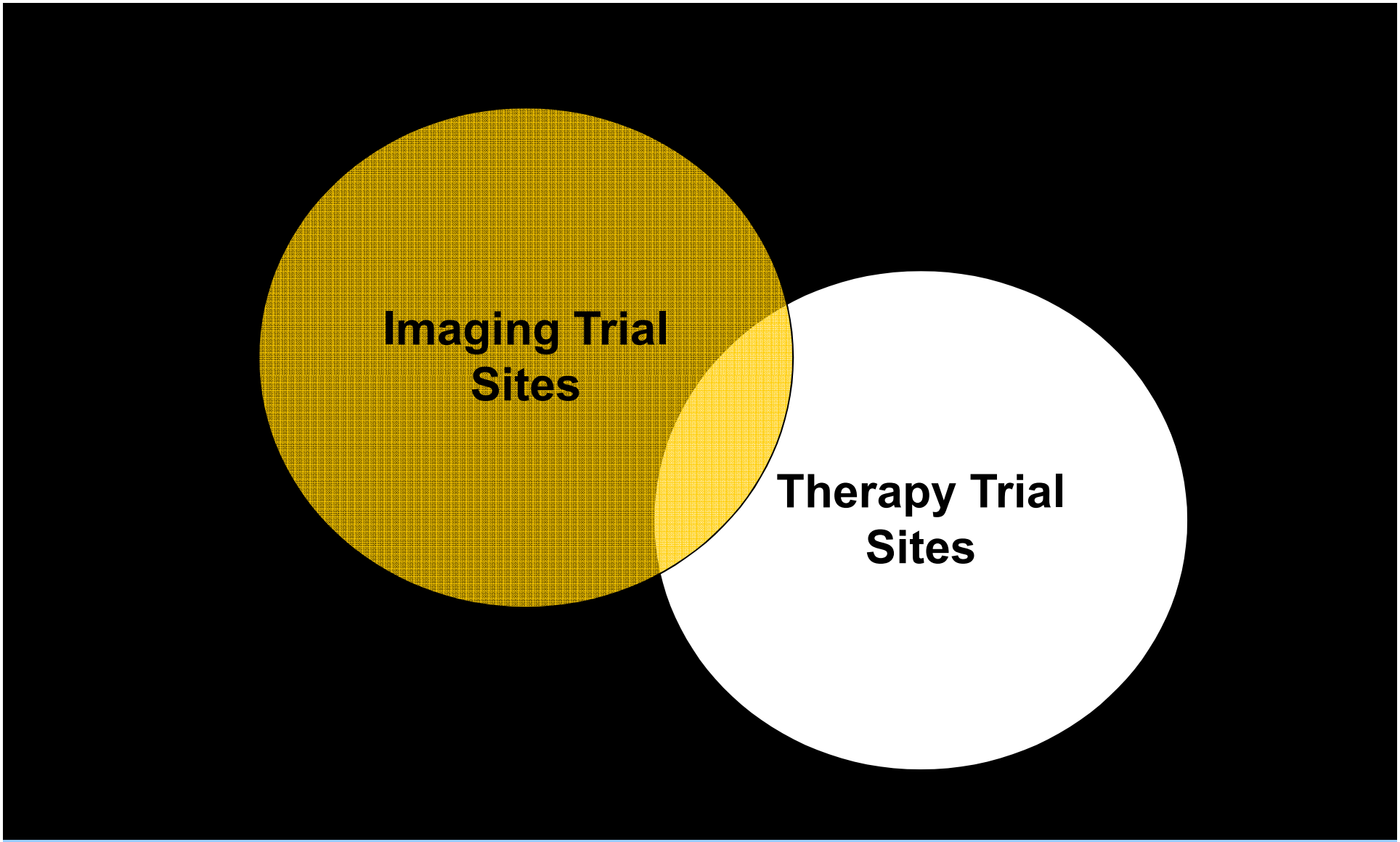

Approach

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- **Focus on critical data points to minimize exposure and facilitate scheduling**
- **Enlarge each Cell of the Venn Diagram**
  - Plan study with as liberal treatment options as possible consistent with the mechanism of the marker tested
  - Balance technical requirements on the imaging sites consistent with study needs
- **Enlarge the "Union"**
  - Focus on sites with clinical / imaging integration
  - Mandate the imaging component in treatment trial

Lessons

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- High quality data quantitative data can be acquired in the setting of multicenter trials
- Site training is key to establishing and maintaining quality
- Accrual into PET biomarker trials is uniquely challenging